FLUTAMIDE- flutamide capsule
Par Pharmaceutical, Inc.

Flutamide Capsules

WARNINGS

Hepatic Injury

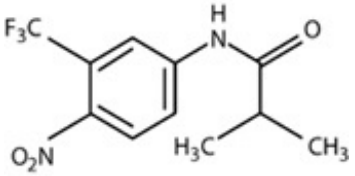
There have been postmarketing reports of hospitalization and rarely death due to liver failure in patients taking flutamide. Evidence of hepatic injury included elevated serum transaminase levels, jaundice, hepatic encephalopathy and death related to acute hepatic failure. The hepatic injury was reversible after discontinuation of therapy in some patients. Approximately half of the reported cases occurred within the initial 3 months of treatment with flutamide.

Serum transaminase levels should be measured prior to starting treatment with flutamide. Flutamide is not recommended in patients whose ALT values exceed twice the upper limit of normal. Serum transaminase levels should then be measured monthly for the first 4 months of therapy, and periodically thereafter. Liver function tests also should be obtained at the first signs and symptoms suggestive of liver dysfunction, e.g., nausea, vomiting, abdominal pain, fatigue, anorexia, “flu-like” symptoms, hyperbilirubinuria, jaundice or right upper quadrant tenderness. If at any time, a patient has jaundice, or their ALT rises above 2 times the upper limit of normal, flutamide should be immediately discontinued with close follow-up of liver function tests until resolution.

DESCRIPTION

Flutamide capsules contain flutamide, an acetanilid, nonsteroidal, orally active antiandrogen having the chemical name, α,α,α-trifluoro-2-methyl-4'-nitrom-propionotoluidide.

Each capsule contains 125 mg flutamide. The compound is a buff to yellow powder with a molecular weight of 276.22 and the following structural formula:



$C_{11}H_{11}F_3N_2O_3$

In addition, each capsule contains the following inactive ingredients: corn starch, lactose monohydrate, magnesium stearate, povidone, and sodium lauryl sulfate. Gelatin capsule shells may contain gelatin, silicon dioxide, sodium lauryl sulfate, titanium dioxide, FDA/E172 Red Iron Oxide, FDA/E172 Yellow Iron Oxide, and black ink containing pharmaceutical glaze (modified) in SD-45, synthetic black iron oxide, N-butyl alcohol, SDA-3A alcohol, FD&C Blue No.2 Aluminum Lake, FD&C Red No.40 Aluminum Lake, FD&C Blue No.1 Aluminum Lake, and D&C Yellow No.10 Aluminum Lake.

CLINICAL PHARMACOLOGY

General

In animal studies, flutamide demonstrates potent antiandrogenic effects. It exerts its antiandrogenic

action by inhibiting androgen uptake and/or by inhibiting nuclear binding of androgen in target tissues or both. Prostatic carcinoma is known to be androgen-sensitive and responds to treatment that counteracts the effect of androgen and/or removes the source of androgen, e.g., castration. Elevations of plasma testosterone and estradiol levels have been noted following flutamide administration.

Pharmacokinetics

Absorption

Analysis of plasma, urine, and feces following a single oral 200 mg dose of tritium-labeled flutamide to human volunteers showed that the drug is rapidly and completely absorbed. Following a single 250 mg oral dose to normal adult volunteers, the biologically active alpha-hydroxylated metabolite reaches maximum plasma concentrations in about 2 hours, indicating that it is rapidly formed from flutamide. Food has no effect on the bioavailability of flutamide.

Distribution

In male rats administered an oral 5 mg/kg dose of ^{14}C-flutamide neither flutamide nor any of its metabolites is preferentially accumulated in any tissue except the prostate. Total drug levels were highest 6 hours after drug administration in all tissues. Levels declined at roughly similar rates to low levels at 18 hours. The major metabolite was present at higher concentrations than flutamide in all tissues studied. Following a single 250 mg oral dose to normal adult volunteers, low plasma concentrations of flutamide were detected. The plasma half-life for the alpha-hydroxylated metabolite of flutamide is approximately 6 hours. Flutamide,*in vivo*, at steady-state plasma concentrations of 24 to 78 ng/mL, is 94% to 96% bound to plasma proteins. The active metabolite of flutamide, in vivo, at steady-state plasma concentrations of 1556 to 2284 ng/mL, is 92% to 94% bound to plasma proteins.

Metabolism

The composition of plasma radioactivity, following a single 200 mg oral dose of tritium-labeled flutamide to normal adult volunteers, showed that flutamide is rapidly and extensively metabolized, with flutamide comprising only 2.5% of plasma radioactivity 1 hour after administration. At least six metabolites have been identified in plasma. The major plasma metabolite is a biologically active alpha-hydroxylated derivative which accounts for 23% of the plasma tritium 1 hour after drug administration. The major urinary metabolite is 2-amino-5nitro-4-(trifluoromethyl)phenol.

Excretion

Flutamide and its metabolites are excreted mainly in the urine with only 4.2% of a single dose excreted in the feces over 72 hours.

Plasma Pharmacokinetics of Flutamide and Hydroxyflutamide in Geriatric Volunteers (mean ± SD)

	Single Dose Flutamide	Hydroxyflutamide	Steady-State Flutamide	Hydroxyflutamide
C_{max} (ng/mL)	25.2 ± 34.2	894 ± 406	113 ± 213	1629 ± 586
Elimination half-life (hr)	---	8.1 ± 1.3	7.8	9.6 ± 2.5
T_{max} (hr)	1.9 ± 0.7	2.7 ± 1.0	1.3 ± 0.7	1.9 ± 0.6
C_{min} (ng/mL)	---	---	---	673 ± 316

Special Populations

Geriatric Following multiple oral dosing of 250 mg t.i.d. in normal geriatric volunteers, flutamide and its active metabolite approached steady-state plasma levels (based on pharmacokinetic simulations) after the fourth flutamide dose. The half-life of the active metabolite in geriatric volunteers after a single

flutamide dose is about 8 hours and at steady-state in 9.6 hours.

Race There are no known alterations in flutamide absorption, distribution, metabolism, or excretion due to race.

Renal Impairment Following a single 250 mg dose of flutamide administered to subjects with chronic renal insufficiency, there appeared to be no correlation between creatinine clearance and either C_{max}or AUC of flutamide. Renal impairment did not have an effect on the C_{max}or AUC of the biologically active alpha- hydroxylated metabolite of flutamide. In subjects with creatinine clearance of < 29 mL/min, the half-life of the active metabolite was slightly prolonged. Flutamide and its active metabolite were not well dialyzed. Dose adjustment in patients with chronic renal insufficiency is not warranted.

Hepatic Impairment No information on the pharmacokinetics of flutamide in hepatic impairment is available (see**BOXED WARNING, Hepatic Injury**).

Women, Pediatrics Flutamide has not been studied in women or pediatric subjects.

Drug-Drug Interactions

Interactions between flutamide capsules and LHRH-agonists have not occurred. Increases in prothrombin time have been noted in patients receiving warfarin therapy (see**PRECAUTIONS**).

CLINICAL STUDIES

Flutamide has been demonstrated to interfere with testosterone at the cellular level. This can complement medical castration achieved with LHRH-agonists which suppresses testicular androgen production by inhibiting luteinizing hormone secretion.

The effects of combination therapy have been evaluated in two studies. One study evaluated the effects of flutamide and an LHRH-agonist as neoadjuvant therapy to radiation in stage B2-C prostatic carcinoma and the other study evaluated flutamide and an LHRH-agonist as the sole therapy in stage D2prostatic carcinoma.

Stage B2-C Prostatic Carcinoma

The effects of hormonal treatment combined with radiation was studied in 466 patients (231 flutamide capsules + goserelin acetate implant + radiation, 235 radiation alone) with bulky primary tumors confined to the prostate (stage B2) or extending beyond the capsule (stage C), with or without pelvic node involvement.

In this multicentered, controlled trial, administration of flutamide capsules (250 mg t.i.d.) and goserelin acetate (3.6 mg depot) prior to and during radiation was associated with a significantly lower rate of local failure compared to radiation alone (16% vs. 33% at 4 years, $P < 0.001$). The combination therapy also resulted in a trend toward reduction in the incidence of distant metastases (27% vs. 36% at 4 years, $P = 0.058$). Median disease-free survival was significantly increased in patients who received complete hormonal therapy combined with radiation as compared to those patients who received radiation alone (4.4 vs 2.6 years, $P < 0.001$). Inclusion of normal PSA level as a criterion for disease-free survival also resulted in significantly increased median disease-free survival in patients receiving the combination therapy (2.7 vs. 1.5 years, $P < 0.001$).

Stage D2Prostatic Carcinoma

To study the effects of combination therapy in metastatic disease, 617 patients (311 leuprolide + flutamide, 306 leuprolide + placebo) with previously untreated advanced prostatic carcinoma were enrolled in a large multicentered, controlled clinical trial.

Three and one-half years after the study was initiated, median survival had been reached. The median actuarial survival time was 34.9 months for patients treated with leuprolide and flutamide versus 27.9 months for patients treated with leuprolide alone. This 7 month increment represents a 25% improvement in overall survival time with the flutamide therapy. Analysis of progression-free survival showed a 2.6

month improvement in patients who received leuprolide plus flutamide, a 19% increment over leuprolide and placebo.

INDICATIONS AND USAGE

Flutamide capsules are indicated for use in combination with LHRH-agonists for the management of locally confined Stage B_2-C and Stage D_2metastatic carcinoma of the prostate.

Stage B_2-C Prostatic Carcinoma

Treatment with flutamide capsules and the goserelin acetate implant should start eight weeks prior to initiating radiation therapy and continue during radiation therapy.

Stage D_2Metastatic Carcinoma

To achieve benefit from treatment, flutamide capsules should be initiated with the LHRH-agonist and continued until progression.

CONTRAINDICATIONS

Flutamide capsules are contraindicated in patients who are hypersensitive to flutamide or any component of this preparation.

Flutamide capsules are contraindicated in patients with severe hepatic impairment (baseline hepatic enzymes should be evaluated prior to treatment).

WARNINGS

Hepatic Injury

SEE BOXED WARNING

Use in Women

Flutamide capsules are for use **only** in men. This product has no indication for women and should not be used in this population, particularly for nonserious or nonlife-threatening conditions.

Fetal toxicity

Flutamide may cause fetal harm when administered to a pregnant woman (see**Pregnancy**).

Aniline toxicity

One metabolite of flutamide is 4-nitro-3-fluoro-methylaniline. Several toxicities consistent with aniline exposure, including methemoglobinemia, hemolytic anemia and cholestatic jaundice have been observed in both animals and humans after flutamide administration. In patients susceptible to aniline toxicity (e.g. persons with glucose-6-phosphate dehydrogenase deficiency, hemoglobin M disease and smokers), monitoring of methemoglobin levels should be considered.

PRECAUTIONS

General

In clinical trials, gynecomastia occurred in 9% of patients receiving flutamide together with medical castration.

Information for Patients

Patients should be informed that flutamide capsules and the drug used for medical castration should be administered concomitantly, and that they should not interrupt their dosing or stop taking these medications without consulting their physician.

Laboratory Tests

Regular assessment of serum Prostate Specific Antigen (PSA) may be helpful in monitoring the patient's response. If PSA levels rise significantly and consistently during flutamide therapy the patient should be evaluated for clinical progression. For patients who have objective progression of disease together with an elevated PSA, a treatment period free of antiandrogen while continuing the LHRH analogue may be considered.

Drug Interactions

Increases in prothrombin time have been noted in patients receiving long-term warfarin therapy after flutamide was initiated. Therefore close monitoring of prothrombin time is recommended and adjustment of the anticoagulant dose may be necessary when flutamide capsules are administered concomitantly with warfarin.

Carcinogenesis and Mutagenesis and Impairment of Fertility

In a 1 year dietary study in male rats, interstitial cell adenomas of the testes were present in 49% to 75% of all treated rats (daily doses of 10, 30, and 50 mg/kg/day were administered). These produced plasma C_{max} values that are 1, 2, 3, and 4 fold respectively, those associated with therapeutic doses in humans. In male rats similarly dosed for 1 year, tumors were still present after 1 year of a drug-free period, but the incidences were 43% to 47%. In a 2 year carcinogenicity study in male rats, daily administration of flutamide at these same doses produced testicular interstitial cell adenomas in 91% to 95% of all treated rats as opposed to 11% of untreated control rats. Mammary adenomas, adenocarcinomas, and fibroadenomas were increased in treated male rats at exposure levels that were 1 to 4 fold those observed during therapeutic dosing in humans. There are likewise reports of malignant breast neoplasms in men treated with flutamide capsules (see **ADVERSE REACTIONS** section).

Flutamide did not demonstrate DNA modifying activity in the Ames Salmonella/microsome -- observed during a 6 week study of flutamide monotherapy in normal human volunteers.

Flutamide did not affect estrous cycles or interfere with the mating behavior of male and female rats when the drug was administered at 25 and 75 mg/kg/day prior to mating. Males treated with 150 mg/kg/day (30 times the minimum effective antiandrogenic dose) failed to mate; mating behavior returned to normal after dosing was stopped. Conception rates were decreased in all dosing groups. Suppression of spermatogenesis was observed in rats dosed for 52 weeks at approximately 3, 8, or 17 times the human dose and in dogs dosed for 78 weeks at 1.4, 2.3, and 3.7 times the human dose.

Animal Toxicology

Serious cardiac lesions were observed in 2/10 beagle dogs receiving 25 mg/kg/day for 78 weeks and 3/16 receiving 40 mg/kg/day for 2 to 4 years. These lesions, indicative of chronic injury and repair processes, included chronic myxomatous degeneration, intra-atrial fibrosis, myocardial acidophilic degeneration, vasculitis and perivasculitis. The doses at which these lesions occurred were associated with 2-hydroxyflutamide levels that were 1 to 12 fold greater than those observed in humans at therapeutic levels.

Pregnancy

Pregnancy Category D

There was decreased 24 hour survival in the offspring of pregnant rats treated with flutamide at doses of 30, 100 or 200 mg/kg/day (approximately 3, 9 and 19 times the human dose). A slight increase in minor variations in the development of the sternebrae and vertebrae was seen in fetuses of rats treated with two higher doses. Feminization of the male rats also occurred at the two higher dose levels. There was a decreased survival rate in the offspring of rabbits receiving the highest dose (15 mg/kg/day, equal to 1.4 times the human dose).

ADVERSE REACTIONS

Stage B_2-C Prostatic Carcinoma

Treatment with flutamide capsules and the goserelin acetate implant did not add substantially to the toxicity of radiation treatment alone. The following adverse experiences were reported during a multicenter clinical trial comparing flutamide + goserelin acetate implant + radiation versus radiation alone. The most frequently reported (greater than 5%) adverse experiences are listed below:

Adverse Events During Acute Radiation Therapy

(within first 90 days of radiation therapy)

	*(n=231) Goserelin Acetate Implant + Fl*utamide + Radiation	*(n=235) Radiation Only*
	% All	% All
Rectum/Large Bowel	80	76
Bladder	58	60
Skin	37	37

Adverse Events During Late Radiation Phase

(after 90 days of radiation therapy)

	*(n=231) Goserelin Acetate Implant + Fl*utamide + Radiation	*(n=235) Radiation Only*
	% All	% All
Diarrhea	36	40
Cystitis	16	16
Rectal Bleeding	14	20
Proclitis	8	8
Hematuria	7	12

Additional adverse event data were collected for the combination therapy with radiation group over both the hormonal treatment and hormonal treatment plus radiation phases of the study. Adverse experiences occurring in more than 5% of patients in this group, over both parts of the study, were hot flashes (46%), diarrhea (40%), nausea (9%), and skin rash (8%).

Stage D_2Metastatic Carcinoma

The following adverse experiences were reported during a multicenter clinical trial comparing flutamide + LHRH agonist versus placebo + LHRH agonist.

The most frequently reported (greater than 5%) adverse experiences during treatment with flutamide capsules in combination with an LHRH agonist are listed in the table below. For comparison, adverse experiences seen with an LHRH agonist and placebo are also listed in the following table.

	(n=294) Flutamide + LHRH agonist	*(n=28) Placebo + LHRH agonist*
	% All	% All
Hot Flashes	61	57
Loss of Libido	36	31
Impotence	33	29
Diarrhea	12	4

Nausea/Vomiting	11	10
Gynecomastia	9	11
Other	7	9
Other GI	6	4

As shown in the table, for both treatment groups, the most frequently occurring adverse experiences (hot flashes, impotence, loss of libido) were those known to be associated with low serum androgen levels and known to occur with LHRH agonists alone.

The only notable difference was the higher incidence of diarrhea in the flutamide + LHRH agonist group (12%), which was severe in 5% as opposed to the placebo + LHRH agonist (4%), which was severe in less than 1%.

In addition, the following adverse reactions were reported during treatment with flutamide + LHRH agonist.

*Cardiovascular System:*hypertension in 1% of patients.

Central Nervous System: CNS (drowsiness/confusion/depression/anxiety/nervousness) reactions occurred in 1% of patients.

Gastrointestinal System: anorexia 4%, and other GI disorders occurred in 6% of patients.

Hematopoietic System: anemia occurred in 6%, leukopenia in 3%, and thrombocytopenia in 1% of patients.

Liver and Biliary System: hepatitis and jaundice in less than 1% of patients.

Skin: irritation at the injection site and rash occurred in 3% of patients.

*Other:*edema occurred in 4%, genitourinary and neuromuscular symptoms in 2%, and pulmonary symptoms in less than 1% of patients.

In addition, the following spontaneous adverse experiences have been reported during the marketing of flutamide: hemolytic anemia,macrocytic anemia,methemoglobinemia, sulfhemoglobinemia, photosensitivity reactions (including erythema, ulceration, bullous eruptions, and epidermal necrolysis) and urine discoloration. The urine was noted to change to an amber or yellow-green appearance which can be attributed to the flutamide and/or its metabolites. Also reported were cholestatic jaundice, hepatic encephalopathy, and hepatic necrosis. The hepatic conditions were often reversible after discontinuing therapy; however, there have been reports of death following severe hepatic injury associated with use of flutamide.

Malignant breast neoplasms have occurred rarely in male patients being treated with flutamide capsules.

Abnormal Laboratory Test Values: Laboratory abnormalities including elevated SGOT, SGPT, bilirubin values, SGGT, BUN, and serum creatinine have been reported.

OVERDOSAGE

In animal studies with flutamide alone, signs of overdose included hypoactivity, piloerection, slow respiration, ataxia, and/or lacrimation, anorexia, tranquilization, emesis, and methemoglobinemia.

Clinical trials have been conducted with flutamide in doses up to 1500 mg per day for periods up to 36 weeks with no serious adverse effects reported. Those adverse reactions reported included gynecomastia, breast tenderness, and some increases in SGOT. The single dose of flutamide ordinarily associated with symptoms of overdose or considered to be life-threatening has not been established.

Flutamide is highly protein bound, and is not cleared by hemodialysis. As in the management of overdosage with any drug, it should be borne in mind that multiple agents may have been taken. If vomiting does not occur spontaneously, it should be induced if the patient is alert. General supportive

care, including frequent monitoring of the vital signs and close observation of the patient, is indicated.

DOSAGE AND ADMINISTRATION

The recommended dosage is 2 capsules 3 times a day at 8 hour intervals for a total daily dose of 750 mg.

HOW SUPPLIED

Flutamide capsules USP, 125 mg, are available as opaque, beige/beige capsules, imprinted “par/753”on the cap and body. They are available in bottle of 180 (NDC 49884-753-13).

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).

INFORMATION FOR PATIENTS

Important information for patients taking flutamide capsules.

Read this information carefully each time your prescription is refilled because there may be new information available. This summary does not tell you everything you need to know about flutamide therapy. Your doctor is the best source of information about your treatment. Ask your doctor about questions you have.

What is flutamide therapy?

Flutamide capsules, in combination with other therapies, is a treatment option for men with some types of prostate cancer.

Prostate cancer results from the abnormal growth of prostate cells. Medical scientists do not know exactly what causes the abnormal cells, but age, environment, and genetics are important factors. Male hormones (“androgens”) cause the cancer to grow. The cancer growth can be slowed down by blocking the effect of androgens.

The flutamide product is used together with an injection called “LHRH agonist,” as a combined treatment called “total androgen blockade.” The goal of this treatment is to reduce androgen levels and to block the effect of androgen on the tumor. The LHRH agonist reduces androgen levels. Flutamide therapy blocks the effect of androgen on the tumor.

Who should not take the flutamide product?

You should not take flutamide capsules if you have liver problems or if you are allergic to it. Flutamide capsules are for use**only**in men, therefore women should not take flutamide capsules.

Are there important risks I should know about flutamide therapy?

Some men taking the flutamide product had liver injury and needed to be hospitalized. In rare cases, men died because of liver failure while they were taking flutamide capsules. In about half of these cases, the liver failure occurred in the first 3 months that they were taking flutamide capsules.

Because the flutamide product may cause liver failure,**it is very important that you have all blood tests recommended by your doctor**. These tests help identify whether you are having liver problems. A recommended schedule for these blood tests is:

- Before starting flutamide treatment.
- Every month for the first 4 months of therapy.
- Periodically after the first 4 months.

In addition, you should**call your doctor right away if you have any of the following signs or symptoms:**

- Loss of appetite.
- Nausea and vomiting.
- Stomach or abdominal pain.
- Fatigue (feeling extremely tired).
- Flu-like symptoms (muscle aches, soreness).
- Brown urine.
- jaundice (yellowing of the skin or whites of the eyes).

These may be signs of liver failure.

How should I take flutamide capsules?

Take your flutamide capsules as your doctor has prescribed. The usual dosing is 2 capsules every 8 hours.

Your doctor will determine whether flutamide therapy is right for you based on many different factors. These include how large your tumor is, how far it has spread and your physical condition. In addition to flutamide capsules, you may be getting other treatments, including regular injections of LHRH agonist or radiation therapy. Do not stop or interrupt any treatment without consulting your healthcare professional.

If you miss a dose of flutamide capsules, simply continue therapy with your next scheduled dose. Do not try to make up for it by taking extra capsules.

Can I take other medicines?

If you are taking any other medicines, especially warfarin (a blood-thinning drug), tell your doctor before beginning flutamide therapy.

What are the other possible side effects of taking flutamide capsules?

In a medical study, when flutamide capsules were taken together with an LHRH agonist, the most common side effects were hot flashes, loss of sex drive (libido) and impotence. In addition, some men had diarrhea, nausea or vomiting, and breast enlargement.

In another medical study, when the flutamide product was taken together with goserelin acetate (an LHRH agonist) and radiation therapy, the side effects of flutamide therapy were about the same as when radiation therapy was given alone. These included hot flashes, diarrhea, nausea and skin rash.

What can I do if I get diarrhea?

If you experience moderate diarrhea due to flutamide capsules, the following advice may help:
- drink plenty of fluids
- reduce your intake of dairy products (for example, milk, cheese, yogurt).
- Increase your intake of whole grains, fruits and vegetables.
- Stop laxative use.
- Take nonprescription antidiarrheal medicines.

If your diarrhea continues or it becomes severe, contact your doctor right away.

Are there any other lab tests my doctor will be performing?

Your doctor may perform other regular tests (such as the PSA blood test) to ensure that your body is responding to treatment. Ask your doctor if you have any questions about how your flutamide therapy is being monitored.

Please ask your doctor about any questions concerning prostate cancer or flutamide therapy, or you can also ask for a more detailed leaflet that is written for healthcare professionals.

Manufactured By:

PAR PHARMACEUTICAL

Chestnut Ridge, NY 10977

PRINCIPAL DISPLAY PANEL- 125 MG/ 180 CAPSULE CONTAINER LABEL

FLUTAMIDE

flutamide capsule

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:49884-753
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
FLUTAMIDE (UNII: 76W6J0943E) (FLUTAMIDE - UNII:76W6J0943E)	FLUTAMIDE	125 mg

Product Characteristics			
Color	BROWN (Beige)	**Score**	no score
Shape	CAPSULE	**Size**	22mm
Flavor		**Imprint Code**	93;7120
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:49884-753-13	180 in 1 BOTTLE; Type 0: Not a Combination Product	01/26/2006	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA075298	01/26/2006	

Labeler - Par Pharmaceutical, Inc. (092733690)

Establishment

Name	Address	ID/FEI	Business Operations
Par Pharmaceutical Inc.		092733690	ANALYSIS(49884-753) , MANUFACTURE(49884-753) , PACK(49884-753)

Revised: 10/2017 Par Pharmaceutical, Inc.